



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 38/17, 39/395, C12N 5/06, A61P 37/00	A3	(11) International Publication Number: WO 00/12113 (43) International Publication Date: 9 March 2000 (09.03.00)
(21) International Application Number: PCT/US99/20026 (22) International Filing Date: 31 August 1999 (31.08.99) (30) Priority Data: 60/098,456 31 August 1998 (31.08.98) US (71) Applicant (for all designated States except US): BIOGEN, INC. [US/US]; 14 Cambridge Center, Cambridge, MA 02142 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): MAGILAVY, Daniel [US/US]; 91 Sherman Street, Cambridge, MA 02140 (US). (74) Agent: KAPLAN, Warren, A.; Biogen, Inc., 14 Cambridge Center, Cambridge, MA 02142 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 29 June 2000 (29.06.00)
(54) Title: METHOD OF MODULATING MEMORY EFFECTOR T-CELLS USING A CD2-BINDING AGENT, AND COMPOSITIONS (57) Abstract Methods of selectively modulating memory effector T lymphocytes in a subject having a medical condition are described. The methods utilize CD2 binding agents.		

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 99/20026

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/17 A61K39/395 C12N5/06 A61P37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 503 648 A (BIOGEN, INC.) 16 September 1992 (1992-09-16) cited in the application the whole document ---	1-63
X	N. DAMLE ET AL.: "Stimulation of cloned human T lymphocytes via the CD3 or CD28 molecules induces enhancement in vascular endothelial permeability to macromolecules with participation of type-1 and type-2 intercellular adhesion pathways." EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 20, no. 9, September 1990 (1990-09), pages 1995-2003, XP000892124 Weinheim, Germany the whole document --- -/-	1-63



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 April 2000

Date of mailing of the international search report

08/05/2000

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Nooi, F

INTERNATIONAL SEARCH REPORT

Int. l. Application No
PCT/US 99/20026

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 06852 A (BIOGEN, INC.) 15 April 1993 (1993-04-15) page 2, line 23 - line 24 examples claims ---	1,3-11, 59-62
X	K. YAMASHITA ET AL.: "A multimeric form of soluble recombinant sheep LFA-3 (CD58) inhibits human T-cell proliferation." IMMUNOLOGY, vol. 92, no. 1, September 1997 (1997-09), pages 39-44, XP002135989 Oxford, GB abstract page 41, right-hand column, line 48 -page 43, left-hand column, line 14 page 43, right-hand column, line 7 - line 8 ---	1-12, 59-62
X	X. PENG ET AL.: "Ligation of CD2 provides a strong helper signal for the production of the type 2 cytokines interleukin-4 and -5 by memory T cells." CELLULAR IMMUNOLOGY, vol. 181, no. 1, 10 October 1997 (1997-10-10), pages 76-85, XP000892106 New York, NY, USA abstract page 83, right-hand column, line 18 -page 84, left-hand column, line 23 ---	1-3,7,8, 12-14, 18-20, 24,25, 29,30, 34,35, 39,40, 44,45, 49,50, 54,55, 59,63
X	J. HOFFMANN ET AL.: "Initiation and perpetuation of rat adjuvant arthritis is inhibited by the anti-CD2 monoclonal antibody (mAb) OX34." ANNALS OF RHEUMATIC DISEASES, vol. 56, no. 12, December 1997 (1997-12), pages 716-722, XP000892112 London, GB abstract page 718, right-hand column, line 14 - line 25 table 1 ----- -/-	1,3,7,8, 13,14, 18-20, 24,25, 29,30, 34,35, 39,40, 44,45, 49,50, 54,55, 59,63

INTERNATIONAL SEARCH REPORT

Int'l. Patent Application No
PCT/US 99/20026

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	G. MAJEAU ET AL.: "Mechanism of lymphocyte function-associated molecule 3-Ig fusion proteins inhibition of T cell responses." THE JOURNAL OF IMMUNOLOGY, vol. 152, no. 6, 15 March 1994 (1994-03-15), pages 2753-2767, XP002135990 Baltimore, MD, USA abstract discussion ----	1-63
A	Y. KASAHARA ET AL.: "Role of interleukin 6 for differential responsiveness of naive and memory CD4+ T cells in CD2-mediated activation." THE JOURNAL OF EXPERIMENTAL MEDICINE, vol. 172, no. 5, 1 November 1990 (1990-11-01), pages 1419-1424, XP000892122 New York, NY, USA abstract ----	1-63
A	P. HOLLSBERG ET AL.: "Increased protein kinase C activity in human memory T cells." CELLULAR IMMUNOLOGY, vol. 149, no. 1, June 1993 (1993-06), pages 170-179, XP000892120 New York, NY, USA abstract ----	1-63
P,X	D. MAGILAVY ET AL.: "Pharmacodynamic effects of LFA3TIP (Amevive) in patients with chronic plaque psoriasis (CPP): Selective modulation of CD45RO+ lymphocytes." JOURNAL OF INVESTIGATIVE DERMATOLOGY, vol. 112, no. 4, April 1999 (1999-04), page 609 XP002136039 Baltimore, MD, USA abstract 518 -----	1-23, 59-63

INTERNATIONAL SEARCH REPORT

International application No.:

PCT/US 99/20026

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-58 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims: it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/20026

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